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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,281	03/06/2002	Vincent Raymond	13587.338	7473

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,281	RAYMOND ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,23,25-33,35-38,40 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-23, 25-33, 35-38, 40, 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed August 5, 2004 has been entered. Claims 22-23, 25-33, 35-38, 40, and 52-56 are pending.

1. The objection of claims 24, 34 and 39 is withdrawn.

2. Claims 22-23, 25-33, 35-38, 40, and 56 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids, which is a polymorphism in a promoter region of the optineurin gene, which are not disclosed in the specification. The genus includes an enormous number of polymorphisms for which no written description is provided in the specification. This large genus is represented in the specification by only the polymorphisms listed in Table 1 (See pg. 18 of the specification) for which data is provided demonstrating an association with the

identification of risk for developing glaucoma or a progression from an ocular hypertensive state and may be associated with therapeutic responsiveness (see pg. 17). Thus, applicant has express possession of only particular polymorphisms listed in Table 1, in a genus, which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations of associating a polymorphism for diagnosing glaucoma by detecting a polymorphism in a promoter region of the optineurin gene is provided. Further, these claims expressly encompass all the different possible allelic variants including insertions, deletion, substitutions and transversions at thousands of different sites. No written description of alleles, of upstream or downstream regions containing additional sequence, which are associated with the polymorphism in a promoter region of the optineurin gene.

The response cited two case laws to argue that in the specification there are enough written descriptions for showing the detailed, relevant identifying characteristics... i.e. complete or partial structure, other physical and or chemical properties and the correlations between function and structure. The response further argues that there are eighteen polymorphisms listed in Table 1. However, SEQ ID NO: 1 has 5054 nucleotides in the sequence. The eighteen polymorphisms listed in Table 1 do not present all thousands polymorphisms of SEQ ID NO: 1. Moreover, the eighteen polymorphism are even not cited in claims. The thousands polymorphisms of SEQ ID NO: 1 for diagnosing glaucoma are not to be envisioned. Thus, the rejection is maintained.

2. Claims 22-23, 25-33, 35-38, 40 and 56 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the marker which is capable of detecting a SNP set forth in Table 2, does not reasonably provide enablement for using any marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and complement thereof, and a complementary nucleic acid molecule obtained from a sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404.

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method for diagnosing glaucoma in a sample obtained from a cell or a body fluid by detecting a polymorphism in a promoter region of the optineurin gene comprising using a marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof, and a complementary nucleic acid molecule

obtained from a sample under nucleic acid hybridization condition, permitting the hybridization and detecting the presence of the polymorphism. The invention is in a class of invention, which has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims encompass any nucleic acid selected from the group consisting of the 5054 nucleotides of SEQ ID NO: 1 which will be used as a marker nucleic acid. Thus, the claims claim 5054 different nucleic acids markers. These species even have less utility in the very large genus for diagnosing glaucoma via detecting a polymorphism in a promoter region of the optineurin gene.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since determination of a use for the many sequences would require, initially, studies to demonstrate some utility or use. This study is an inventive, unpredictable and difficult undertaking in itself, and utility would need to be demonstrated by some association such as an epidemiological study. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art in biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. For example, In Rezaie et al (Science, 2002, Vol. 295(8)), Rezaie et al. indicate that the identification of *OPTN* as an adult-onset glaucoma gene

provides an opportunity to screen the general population because *OPTN* mutations are a contributing factor in patients with normal pressure glaucoma (NPG) (See pg. 1079, column 2, last paragraph). However, Rezaie et al. do not disclose a nucleic acid marker having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof, and a complementary nucleic acid molecule obtained from a sample.

Working Examples

The specification has a working example of the identification of SNPs in the optineurin promoter. The method applies genomic DNA from 23 individuals sequenced (See pg. 111-113). Nevertheless, the method does not apply the marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof and a complementary nucleic acid molecule obtained from a sample.

Guidance in the Specification.

The specification provides no guidance on uses for the marker nucleic acid.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high (see Rezaie et al.), the specification provides one with no written description or guidance that leads one to a reliable method of using the marker nucleic acids for diagnosing glaucoma in a sample obtained from a cell by detecting a polymorphism in a promoter region of the optineurin gene,One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the

unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

The response argues that there are Example 1 and table 4 in the specification (See pg 112 of the specification) which indicate that the specification provides ample guidance. However, example 1 and table 4 do not present that all eighteen polymorphisms are used for detecting glaucoma. There are only three polymorphisms used for the allelic frequencies calculation in patients and controls. Moreover, among these three polymorphisms, the locations 391 and 887 of the polymorphisms do not show the frequencies, which are very different between Primary Open Angle Glaucoma and Normal (control) (See pg. 112, Table 4). Therefore, it cannot envision the enablement for diagnosing glaucoma via the calculation of the allelic frequencies. Thus the rejection is maintained.

3. The newly added claims 52-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the marker which is capable of detecting a SNP at location 709 as set forth in Table 4, does not reasonably provide enablement for using any polymorphisms of SEQ ID NO: 1 and a complementary nucleic acid molecule obtained from a sample as cited in claims 52 and 54 for diagnosing glaucoma via detecting the single nucleotide polymorphism of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims.

Summary

4. No claims are allowable.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung
October 18, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
10/20/04